SHOCK, Vol. 32, No. 6, pp. 565–571, 2009

RAPID PREDICTION OF TRAUMA PATIENT SURVIVAL BY ANALYSIS OF HEART RATE COMPLEXITY: IMPACT OF REDUCING DATA SET SIZE

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Received 23 Jan 2009; first review completed 10 Feb 2009; accepted in final form 8 Apr 2009

ABSTRACT—Heart rate complexity (HRC) is an emerging "new vital sign" for critically ill and injured patients. Traditionally, 800-beat data sets have been used to calculate HRC variables, thus limiting their practical use in an emergency. We sought to investigate whether data set reductions diminish the use of HRC to predict mortality in prehospital trauma patients. Ectopy-free, 800-beat sections of electrocardiogram (EKG) were collected from 31 prehospital trauma patients during their helicopter transport to a level 1 trauma center. Twenty patients survived (survivors) and 11 died (nonsurvivors) after admission. HRC was assessed via approximate entropy (ApEn), sample entropy (SampEn), and similarity of distributions (SOD). The amplitude of high-frequency oscillations was measured via the method of complex demodulation. This analysis was repeated in data sets of 800, 600, 400, 200, and 100 beats. For 800 beats, ApEn and SampEn were lower in nonsurvivors than in survivors, and SOD was higher. With data set reduction, ApEn in survivors and nonsurvivors gradually approached each other but remained different until the 200-beat dataset. Sample entropy did not change with data shortening and remained lower in nonsurvivors in all data sets. Similarity of distributions was nearly constant within groups for all data sets and discriminated survivors from nonsurvivors in 800- and 100-beat data sets. High-frequency amplitude distinguished survivors from nonsurvivors in 400-, 200-, and 100-beat data sets. Logistic regression was performed for the 800-, 200-, and 100-beat data sets, retaining SampEn as a predictor of mortality (area under the receiver-operating-characteristic curves, 0.821–0.895). HRC decreased in nonsurvivors versus survivors. This finding was confirmed for data sets as short as 100 beats by computationally different metrics. SampEn, SOD, and complex demodulation were relatively unaffected by data set reduction. These metrics may be useful for rapid identification of trauma patients with potentially lethal injuries using short EKG data sets.

KEYWORDS—Wounds and injuries, transportation of patients, electrocardiography, complexity, nonlinear analysis, spectrum analysis

INTRODUCTION

The battlefield represents one extreme example of the problems faced by all those who care for patients in the prehospital and critical care environments. During combat casualty care, medics must make rapid and accurate triage decisions under hostile conditions—darkness, severe weather, and, most importantly, threat of enemy fire. In this environment, the weight and cube of equipment that medics bring to the casualty is constrained by what they can carry on their backs. Furthermore, the desire to reduce the risk to the medic's life by not sending him or her to rescue a casualty who may be minimally injured or dead until the scene is safe has generated a search for techniques that can facilitate remote triage. This concept envisions acquisition of data by sensors (such as electrocardiographic leads) worn by soldiers and transmission of the data by telemetry to the medic. These requirements—better diagnostic tools for the combat medic and remote monitoring and triage devices for soldiers—have motivated a search for new approaches to the diagnosis of shock in combat casualties that extract as much information content as possible from, for example, the electrocardiogram (EKG).

One approach to this type of signal analysis, called frequency-domain analysis, uses fast Fourier transform (FFT) or similar methods to quantify the strength of the regular oscillations present in the heart rate. Of these oscillations, the most well known is the respiratory sinus arrhythmia, that is, oscillations that occur at the same frequency as the respiratory rate. By this method, an EKG that has a pronounced respiratory sinus arrhythmia has an elevated high-frequency power compared with an EKG that varies little. This type of heart-rate variability analysis, however, suffers from a variety of methodological limitations such as high susceptibility to the presence of ectopic beats and to nonstationarity (changes in the mean and SD of the heart rate during the data set analyzed). In addition, such methods say little about nonregular variability in the heart rate.

A different approach to signal analysis uses statistics derived from nonlinear dynamics. Broadly speaking, these statistics quantify the structural complexity of the heart-rate time series. In so doing, they aim to describe the underlying complexity, and thus, the health, of the cardiovascular regulatory system (1–12). Several studies have shown that reduction of heart-rate complexity (HRC) is a sensitive indicator of physiologic deterioration (2, 4, 7, 11) and suggest the use

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This study was supported by the Combat Casualty Care Research Program and the Telemedicine and Advanced Technology Research Center, US Army Medical Research and Materiel Command.

DOI: 10.1097/SHK.0b013e3181a993dc

Report Documentation Page

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
01 DEC 2009	**N/A**	**-**

4. TITLE AND SUBTITLE	5a. CONTRACT NUMBER
Rapid prediction of trauma patient survival by analysis of heart rate complexity: impact of reducing data set size	5b. GRANT NUMBER
	5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S)	5d. PROJECT NUMBER
Batchinsky A. I., Salinas J., Kuusela T., Necsoiu C., Jones J., Cancio L. C.,	5e. TASK NUMBER
	5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)	8. PERFORMING ORGANIZATION REPORT NUMBER
United States Army Institute of Surgical Research, JBSA Fort Sam Houston, TX 78234	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)	10. SPONSOR/MONITOR'S ACRONYM(S)
	11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release, distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			
unclassified	**unclassified**	**unclassified**	**UU**	**7**	

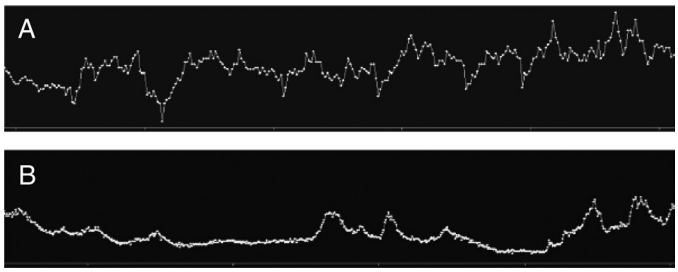

FIG. 1. **Examples of RRI time series for a survivor (top) and a nonsurvivor (bottom)**. These waveforms were generated by determining the instantaneous RRI on a beat-by-beat basis and plotting it as a function of time. The differing amounts of complex variability present in the two waveforms can be quantified by the nonlinear statistics described in the text. Horizontal axis represents time (250 s for both signals), whereas vertical axis represents mean RRI.

of HRC as a "new vital sign" for remote monitoring and decision support in the field (4, 11, 13).

We previously applied the complexity approach to the analysis of the heart-rate time series in patients en route to a level 1 trauma center and reported that decreased HRC in the prehospital setting correlates with death (11) and with the performance of life-saving interventions in these patients (14) (Fig. 1). However, HRC measurements traditionally are applied to large data sets containing at least 800 R-to-R intervals (RRIs) which, furthermore, should be relatively free of ectopy or noise. Thus, the use of this approach in emergency situations may be limited by time constraints or by inability to get clean data sets of sufficient duration. Under these circumstances, a "snapshot" of the casualty's state from a shorter segment of EKG data may be all that is realistically available for early decision support.

The objective of this study was to investigate whether data set length reductions diminish the use of new vital signs derived from HRC to predict mortality in prehospital trauma patients and to determine the smallest data set useful for this prediction. To this end, we reanalyzed EKGs of prehospital trauma patients from a previously reported study (11). We began with the data sets of 800 heartbeats in length used in the previous study and examined progressively shorter data sets within the original 800 beats. We hypothesized that the ability of HRC techniques to discriminate between survivors and nonsurvivors would be retained despite progressive data set size reduction from 800 to at least 200 beats (15).

MATERIALS AND METHODS

This study involved analysis of EKGs and clinical data from the Trauma Vitals database, housed at the US Army Institute of Surgical Research (Fort Sam Houston, Tex). The database stores prehospital patient data from point of injury until delivery via Life Flight helicopter to Memorial Hermann Hospital, a regional level 1 trauma center in Houston (11, 16, 17). A ProPaq 206EL vital signs monitor (WelchAllyn, Inc., Skaneateles Falls, NY) and a standard run sheet were used for data collection onboard the aircraft. Continuous EKG waveforms were acquired from the monitor to an iPAQ personal digital assistant (Talla-tech RPDA, Tallahassee, Fla) and were recorded at a sampling frequency of 186 Hz. Thirty-one EKG recordings free of electromechanical noise (severe enough to prevent R-wave identification), free of ectopic beats, and at least 800 heartbeats in length were available for analysis. Vital signs, mechanism of injury (blunt or penetrating), field total Glasgow Coma Scale score (GCS_{TOTAL}), and the motor component of the score (GCS_{MOTOR}), age, sex, and demographics were recorded (11).

EKG analysis

From each subject, data sets containing 800 RRIs were obtained, imported into WinCPRS software (Absolute Aliens Oy, Turku, Finland), and analyzed as a single discrete data set as previously reported (11). Automatic identification of R waves was performed by the software and manually verified in every data set. The person performing analyses was blinded to patient outcomes. All variables were calculated as described previously (see succeeding sentences) (1, 4). Identical analysis was then performed in data sets containing 600, 400, 300, 200, and 100 RRIs. Each of the shorter data sets was created within the original 800-beat set by equidistant shortening of the 800-beat data set toward the middle of the file. The following variables (explained in greater detail in the Discussion) were calculated in all investigated data sets:

1. Approximate entropy (ApEn) (18) and sample entropy (SampEn) (15). For both ApEn and SampEn calculations, the dimension parameter m was 2, and the filter parameter r was 20% of the SD (1).
2. Fractal dimension by curve lengths (FDCL) and by dispersion analysis (FDDA) (1).
3. Detrended fluctuation analysis (DFA) (19). In this study, we calculated the short-term (4–10 RRIs) scaling exponent by DFA.
4. Similarity of distributions (SOD), which calculates the probability of similar RRI signal-amplitude distributions as a function of time (11, 20).
5. Symbol-dynamics indices: percentage of forbidden words, bit-per-word entropy (BPWEn), and symbol distribution normalized entropy (DisnEn) (1, 4, 21, 22).
6. Signal stationarity (StatAv), which assesses whether the mean and SD of the signal change over time in each data set (22).
7. Frequency-domain and time-domain variables: although the focus in this study was on nonlinear techniques, we also calculated the low-frequency power (LF; RRI spectral power at low-frequency range, 0.05–0.15 Hz) and high-frequency power (HF; frequency range, 0.15–0.4 Hz) of heart-rate oscillations using FFT (4), and the amplitude of low- (LFA) and high-frequency oscillations (HFA) using complex demodulation (CDM). The HF and HFA variables correlate with vagal cardiac control, whereas the LF and LFA variables describe both vagal and sympathetic inputs to the heart. In addition, standard time-domain measures are also reported.

Statistical analysis

SAS version 9.1 (SAS Institute, Cary, NC) was used. In each data set, univariate analysis was performed using two samples, Student t test or Mann-Whitney U test, as appropriate. Multiple logistic regressions with stepwise selection and likelihood ratio tests were performed to identify independent predictors of mortality of all available EKG-derived metrics. We chose variables with a P value of less than 0.2 by univariate analysis as candidates for the logistic models. SampEn, rather than ApEn, was used in this analysis because of the high correlation between these two variables in the 800-beat data set (11). This was done to allow for comparison of the discriminatory power of SampEn in data sets progressively shorter than 800 beats. The Hosmer-Lemeshow goodness-of-fit test was used to estimate the regression model fit. Receiver-operating-characteristic (ROC) curves were constructed to assess the diagnostic performance of predictive equations. Estimated odds ratios and their 95% confidence intervals (CIs) were determined by the

TABLE 1. **Demographics and vital signs**

Variable	NonS	S
Age, yr	43.36 ± 5.79	38.10 ± 3.40
Sex	M (7), F (4)	M (15), F (5)
MOI	B (6), P (5)	B (13), P (7)
HR	117.46 ± 8.54	99.63 ± 4.39
MAP	74.62 ± 9.54	82.7 ± 4.84
GCS_{TOTAL}	8.64 ± 1.70*	13.17 ± 0.82
GCS_{MOTOR}	3.36 ± 0.72†	5.50 ± 0.32

Data are mean ± SEM. For "Sex" and "MOI" variables, a chi-square test was used. Asterisks and daggers denote significance levels among groups by two samples, Student t test or Mann-Whitney U test: *$P < 0.05$, †$P < 0.01$.

B indicates blunt; GCS_{MOTOR}, field Glasgow Coma Score motor; GCS_{TOTAL}, field Glasgow Coma Score total; HR, heart rate; MOI, mechanism of injury; NonS, non-survivors; P, penetrating; S, survivors.

TABLE 2. **Nonlinear analysis results**

Variable	Group	800 Heartbeats	600 Heartbeats	400 Heartbeats	200 Heartbeats	100 Heartbeats
ApEn	NonS	0.87 ± 0.06†	0.89 ± 0.05*	0.85 ± 0.05*	0.76 ± 0.05*	0.66 ± 0.04
	S	1.09 ± 0.04	1.07 ± 0.04	1.02 ± 0.03	0.87 ± 0.02	0.69 ± 0.03
SampEn	NonS	0.80 ± 0.08†	0.83 ± 0.07†	0.83 ± 0.08*	0.83 ± 0.08†	0.83 ± 0.10†
	S	1.1 ± 0.05	1.12 ± 0.06	1.16 ± 0.06	1.20 ± 0.07	1.23 ± 0.09
DFA	NonS	0.94 ± 0.14*	0.92 ± 0.14	0.93 ± 0.14	0.84 ± 0.13	0.78 ± 0.10
	S	1.26 ± 0.08	1.21 ± 0.08	1.23 ± 0.07	1.01 ± 0.07	0.90 ± 0.08
FDCL	NonS	1.66 ± 0.05	1.68 ± 0.05	1.67 ± 0.05	1.68 ± 0.04	1.69 ± 0.05
	S	1.72 ± 0.02	1.73 ± 0.02	1.74 ± 0.02	1.75 ± 0.03	1.75 ± 0.04
FDDA	NonS	1.08 ± 0.02*	1.13 ± 0.04	1.10 ± 0.02*	1.14 ± 0.03	1.15 ± 0.02
	S	1.13 ± 0.01	1.17 ± 0.03	1.16 ± 0.02	1.17 ± 0.02	1.20 ± 0.03
SOD	NonS	0.28 ± 0.04*	0.28 ± 0.04	0.28 ± 0.04	0.28 ± 0.04	0.29 ± 0.05*
	S	0.19 ± 0.02	0.20 ± 0.02	0.20 ± 0.02	0.19 ± 0.02	0.19 ± 0.02
FW	NonS	51.46 ± 4.91	52.91 ± 4.21	53.09 ± 4.04	56.00 ± 3.05	66.00 ± 3.13
	S	52.55 ± 2.28	52.30 ± 2.56	50.20 ± 2.27	56.00 ± 1.95	60.85 ± 1.94
DisnEn	NonS	0.62 ± 0.04	0.61 ± 0.03	0.63 ± 0.03	0.64 ± 0.03	0.61 ± 0.04
	S	0.65 ± 0.02	0.66 ± 0.01	0.69 ± 0.01	0.67 ± 0.02	0.67 ± 0.02
BPWEn	NonS	3.73 ± 0.22	3.66 ± 0.20	3.79 ± 0.19	3.85 ± 0.19	3.69 ± 0.25
	S	3.91 ± 0.09	3.98 ± 0.08	4.11 ± 0.07	4.02 ± 0.10	4.01 ± 0.10
StatAv	NonS	0.89 ± 0.05	0.83 ± 0.07	0.82 ± 0.06	0.73 ± 0.06‡	0.66 ± 0.04‡
	S	0.82 ± 0.03	0.79 ± 0.02	0.74 ± 0.03§	0.67 ± 0.04§	0.59 ± 0.04§

All variables measured in arbitrary units except FW. Data are mean ± SEM.
Asterisks and daggers denote significance levels among groups by 2 samples, Student *t* test or Mann-Whitney *U* test, respectively: **P* < 0.05; †*P* < 0.01. Significance of StatAv changes for survivors (§) and nonsurvivors (‡) at each data set when compared with 800 beats by one-way ANOVA with repeated measures, *P* < 0.05.
ApEn indicates approximate entropy; BPWEn, bit-per-word entropy; DisnEn, normalized symbol-dynamics entropy; DFA, detrended fluctuation analysis; FDCL, fractal dimension by curve lengths; FDDA, fractal dimension by dispersion analysis; FW, percentage of forbidden words (%); NonS, nonsurvivors; S, survivors; SampEn, sample entropy; SOD, similarity of distributions; StatAv, stationarity.

maximum likelihood method. The change in the Pearson chi-square statistic due to deleting an individual observation was used to detect ill-fitted observations or outliers. If the model excluding outliers and influential cases had a classification accuracy rate that was better than the baseline model that included all cases, the revised model was used.

RESULTS

Demographic data and vital signs are reported in Table 1. In brief, survivors differed from nonsurvivors with respect to GCS_{TOTAL} and GCS_{MOTOR}, both of which were lower in nonsurvivors. Trends toward a higher heart rate and lower MAP were present, but these trends were not statistically significant (11).

In the 800-beat data sets, the nonlinear measures, to include ApEn, SampEn, FDDA, and DFA, were statistically lower in nonsurvivors than in survivors, and SOD was higher. FDCL, DisnEn, and BPWEn were not different between

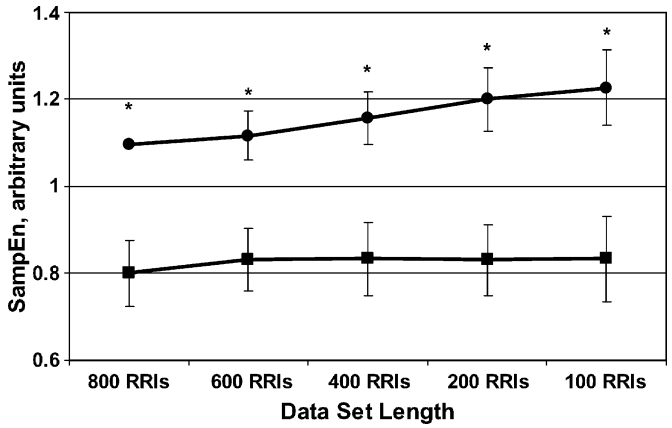

FIG. 2. **Separation of survivors and nonsurvivors in data sets of different lengths using SampEn**. Circles denote survivors, and squares indicate nonsurvivors. Data are mean ± SEM. Statistical analysis by Mann-Whitney *U* test: **P* < 0.05.

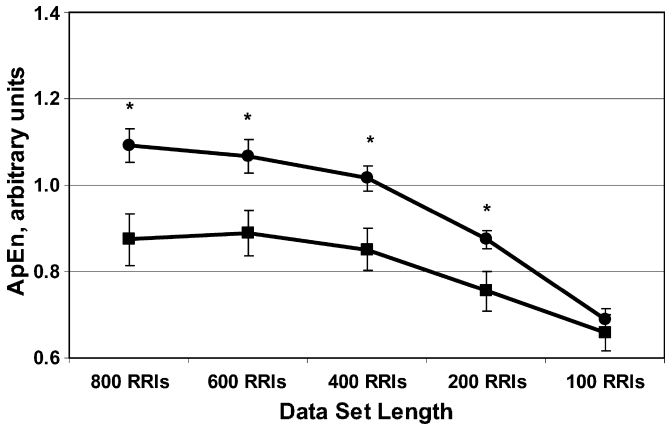

FIG. 3. **Separation of survivors and nonsurvivors in data sets of different lengths using ApEn**. Circles denote survivors, and squares indicate nonsurvivors. Data are mean ± SEM. Statistical analysis *t* test: **P* < 0.05.

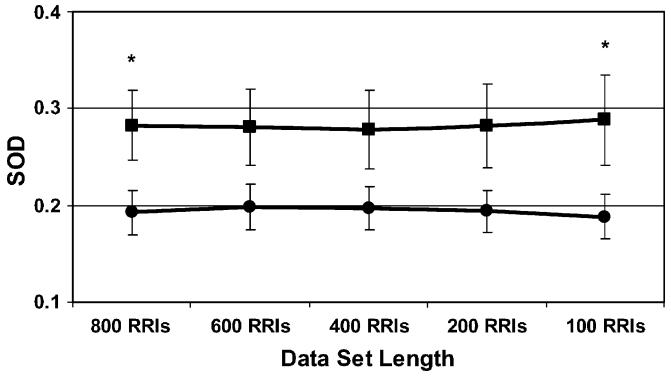

FIG. 4. **Separation of survivors and nonsurvivors in data sets of different lengths using SOD**. Circles denote survivors, and squares indicate nonsurvivors. Data are mean ± SEM. Statistical analysis *t* test: $^*P < 0.05$.

nonsurvivors and survivors at any time scale. Although StatAv did not differ between groups at any time scale, it did increase with shortening of data sets within groups, that is, the data sets became more stationary as they became shorter (Table 2).

With data set size reduction, ApEn in survivors and nonsurvivors gradually approached each other but remained statistically different down to a data set size of 200 beats (Fig. 2). In contrast, SampEn did not change in either group with data set shortening and remained significantly lower in nonsurvivors in all data sets (Table 2, Fig. 3).

DFA separated the nonsurvivors from the survivors in the 800-beat data sets but not in the other data sets. FDDA was lower in nonsurvivors in the 800- and 400-beat data sets. SOD retained discriminatory power among groups in the 800- and 100-beat data sets (Table 2, Fig. 4). With respect to the time- and frequency-domain results, LF (by FFT) varied widely within groups with data set reduction and was higher in survivors in 100-beat data sets (Table 3). In contrast, HFAs (by CDM) were fairly constant within groups across all time scales evaluated. CDM HFA distinguished between survivors and nonsurvivors for 400-, 200-, and 100-beat data sets. None of the other time- or frequency-domain measures discriminated between the groups at any of the investigated time scales (Table 3).

Association with mortality

Logistic regression was used to determine independent predictors of mortality using RRI-derived metrics with a univariate *P* value less than 0.2. A separate equation was calculated for data sets of 800, 200, and 100 beats in duration. All three of these analyses retained SampEn as an independent predictor of mortality, but with different equation coefficients for each data set (Table 4). The area under the ROC curve was 0.895 for the 800-beat equation, 0.895 for the 200-beat equation, and 0.821 for the 100-beat equation (Fig. 5). Comparison of ROC curves from 800-, 200-, and 100-beat data sets did not reveal a statistical difference among the curves ($P = 0.57$).

DISCUSSION

We investigated the impact of data set length reduction on the ability of variables derived from HRC analysis to

TABLE 3. **Time domain, frequency domain (FFT), and CDM results**

Variable	Group	800 Heartbeats	600 Heartbeats	400 Heartbeats	200 Heartbeats	100 Heartbeats
RRI, mean	NonS	543.91 ± 47.37	543.09 ± 45.69	545.00 ± 46.69	546.18 ± 47.98	546.09 ± 48.77
	S	626.30 ± 29.47	625.50 ± 29.60	626.65 ± 29.55	626.35 ± 29.14	627.10 ± 28.66
RRI, SD	NonS	27.64 ± 10.52	24.82 ± 9.06	21.64 ± 7.68	15.64 ± 5.31	13.27 ± 4.96
	S	24.90 ± 3.64	23.10 ± 3.50	21.25 ± 3.35	19.95 ± 3.14	18.35 ± 3.00
RMSSD	NonS	8.09 ± 2.16	7.45 ± 1.54	7.73 ± 1.72	8.00 ± 1.96	7.45 ± 1.67
	S	11.60 ± 1.99	12.20 ± 2.13	12.35 ± 2.13	12.15 ± 2.04	12.55 ± 2.15
pNN50	NonS	0.38 ± 0.36	0.26 ± 0.24	0.35 ± 0.32	0.55 ± 0.50	0.27 ± 0.19
	S	1.22 ± 0.99	1.59 ± 1.04	1.64 ± 1.09	1.53 ± 0.96	1.72 ± 0.94
TP	NonS	1672.55 ± 1325.23	755.55 ± 568.76	575.73 ± 423.26	315.73 ± 221.36	252.55 ± 159.11
	S	576.35 ± 151.55	570.55 ± 179.93	526.85 ± 170.26	487.20 ± 164.12	458.80 ± 189.69
LF	NonS	174.64 ± 75.12	192.36 ± 149.08	183.64 ± 138.59	113.00 ± 70.13	87.45 ± 53.32*
	S	233.00 ± 62.22	177.25 ± 57.14	168.95 ± 53.06	157.45 ± 49.82	153.20 ± 49.66
HF	NonS	44.46 ± 17.83	28.27 ± 23.28	26.55 ± 21.86	22.18 ± 17.40	16.64 ± 11.89
	S	73.05 ± 26.03	63.75 ± 31.01	62.25 ± 28.83	56.15 ± 21.59	49.85 ± 17.62
CDM LFA	NonS	9.09 ± 4.15	9.18 ± 4.25	8.55 ± 3.75	8.27 ± 3.66	7.82 ± 3.03
	S	13.10 ± 2.11	12.65 ± 2.08	12.95 ± 2.05	12.85 ± 2.00	12.40 ± 2.10
CDM HFA	NonS	3.27 ± 1.05	3.27 ± 0.96	3.18 ± 1.08*	3.27 ± 1.16*	3.09 ± 1.00*
	S	6.15 ± 1.24	6.30 ± 1.32	6.70 ± 1.37	6.45 ± 1.24	6.45 ± 1.29

Data are mean ± SEM. Statistical analysis by Mann-Whitney *U* test: $^*P < 0.05$.
CDM HFA indicates amplitude of the HF oscillations; CDM LFA, amplitude of the LF oscillations; HF, RRI spectral power at high frequency (0.15 – 0.4 Hz ms^2); LF, RRI spectral power at the low frequency (0.05 – 0.15 Hz ms^2); pNN50, percentage of R-R intervals that vary by at least 50 ms; NonS, nonsurvivors; RRI, mean, mean R-to-R interval of the EKG; RRI, SD, standard deviation of RRI; RMSSD, root mean square of SD; S, survivors; TP, total R-to-R interval spectral power (0.003 – 0.4 Hz ms^2).

TABLE 4. **Logistic regression equations for prediction of mortality calculated from data sets containing 800, 200, and 100 heartbeats**

Data set length	Equation	Odds ratio	95% CI for odds	Area under ROC	Asymptotic significance	95% CI
800 beats	$K = 8.247–9.544$ (SampEn)	0.00007	0–0.124	0.895	0.001	0780–1.010
200 beats	$K = 6.881–7.708$ (SampEn)	0.00045	0–0.159	0.895	0.001	0.781–1.000
100 beats	$K = 3.142–3.748$ (SampEn)	0.024	0.001–0.494	0.821	0.005	0.662–0.980

In all data sets, SampEn was retained as the only independent predictor of death. P (death) = e^k / 1 + e^k, where k is given by the previously mentioned equations for the different data sets.

distinguish eventual survivors from nonsurvivors in prehospital trauma patients. The principal finding is that, whereas HRC variables are typically calculated using data sets of 800 beats or more in length, several of these variables, which include SampEn, can provide meaningful clinical results using data sets as short as 100 beats in length. Reasonably high areas under the ROC curve (0.821–0.895) were obtained for SampEn as an independent predictor of mortality despite data set length reduction. We also found that a complexity metric, SOD, and HFA by CDM retained the ability to differentiate survivors from nonsurvivors in the smallest data sets. These results suggest that prediction of mortality using these tools may be technically feasible in prehospital and emergency situations, and that HRC may provide meaningful information after approximately 1 min of EKG monitoring. Although trends in the expected direction were present in the traditional vital signs (higher heart rate and lower MAP), these trends were not statistically significant—indicating the potential superiority of the HRC-based "new vital signs."

HRC analysis uses tools from nonlinear dynamics and complex systems theory to quantify various aspects of the structure of the RRI time series (23, 24). Why should this approach be superior to simply measuring the traditional vital signs? Tracking changes in one component of a complex system (such as the heart rate) may lead to insight into the dynamics of the whole system (such as the health of the cardiovascular system in a trauma patient) (25) and, potentially, allow prediction of the near-future state as well. There are several approaches to this type of analysis.

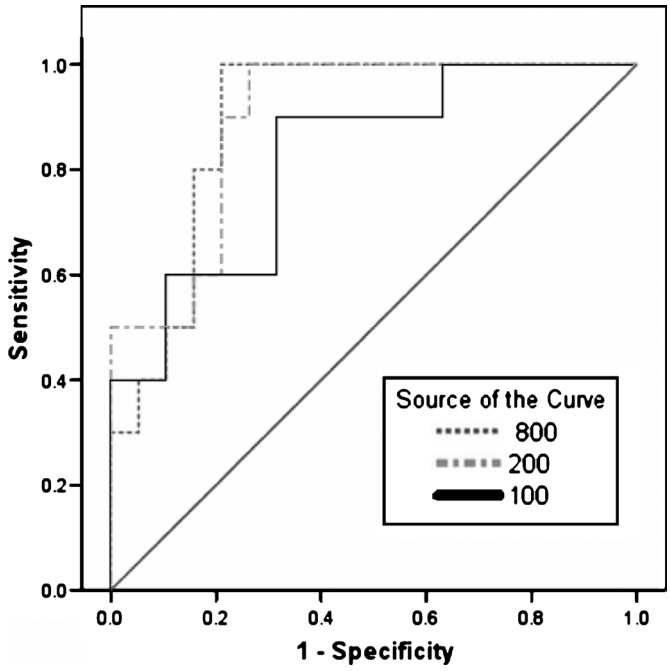

FIG. 5. **Receiver-operating-characteristic curves for prediction of mortality using logistic regression equations derived from 800-, 200-, and 100-beat-long data sets (for areas under the curve, see Table 3).**

Entropy

Assessment of HRC from the RRI time series is possible with tools that investigate the information content or degree of randomness within the signal. For this purpose, we used ApEn (18) and SampEn (15). Both ApEn and SampEn explore the amount of information embedded in the data that defines the next pattern in the time series. In other words, if the time series is random and the next pattern in the data set is not predictable from the previous section within the data, the signal carries high information content, is unpredictable, and is high in entropy. This concept is illustrated in Figure 1A, which shows the time series of a survivor that is characterized by a visibly more random signal pattern. In contrast, Figure 1B depicts a nonsurvivor in whom the next section in the data is predictable and the system's information content is decreased.

In the 800-beat data sets in the present study, nonsurvivors had significantly lower ApEn and SampEn than survivors. This finding is consistent with reports of decreased HRC as measured by ApEn and/or SampEn during hypotension (22) and hemorrhagic shock in animals (3, 4) as well as during burn shock (12). Whereas measurement of SampEn has been reported to be feasible with data sets as short as 200 points (15), in the present study, separation of the two groups of patients based on SampEn was retained down to 100-beat data sets (Fig. 2). As shown by the ROC curve comparison of the 800-, 200-, and 100-beat equations, association with mortality was reasonably accurate and comparable in all three data sets (Fig. 5). This finding is new and suggests that, in settings in which longer sections of EKG cannot be obtained, SampEn may still be useful. The ApEn method has not been suggested for use in data sets shorter than 800 beats based on methodological grounds (1, 18). Indeed, our findings indicate decreasing separation between the groups with smaller and smaller data sets (Fig. 3).

Fractal dimension

Goldberger and West (24, 26) introduced the concept of fractals, or self-similarity at multiple scales, to physiology and medicine. They argued that the fractal architecture of a physiologic signal such as the heart rate may convey important information regarding the underlying dynamics of the system,

and that alterations in fractal scaling may reflect physiologic deterioration. Such self-similarity may characterize a signal over long and/or short ranges, and thus can be quantified by correlations over different time scales. In other words, trends in a heart-rate time series may depend not only on recent events but also on remote events—constituting a "memory effect" (24).

In this study, we used three fractal metrics. The first, FDCL, assesses the fractal dimension of the signal by subdividing each signal section into short segments and counting the number of these short segments that are necessary to follow the signal line. FDCL failed to separate survivors from nonsurvivors in all investigated data sets.

The second method used, FDDA, differs from FDCL in that a new signal is created from the means of adjacent values in the original signal, and the SEM is plotted against the means on a log-log scale. FDDA distinguished among the groups at 800 and 400 beats. The third fractal measure determines power-law correlations within a detrended signal (19). DFA was used to reveal short-term correlations within the data on a 4- to 8-beat scale. In this study, DFA separated survivors versus nonsurvivors in the 800-beat sections of EKG but not in the shorter data sets.

These findings are complementary to the identification of lower HRC by entropy metrics because both methods are different ways of quantifying a more regular structural organization of the signal in life-threatening states. Longer data sets will be required to increase the utility of fractal metrics.

Similarity of distribution

The SOD method begins with division of the RRI time series into arbitrary time windows and converts the RRI signal within each window into a histogram (amplitude distribution). It then investigates the probability that similar RRI histograms will recur in each time window. No overlap in the histograms yields an SOD of 0 and perfect overlap, an SOD of 1 (20). We became interested in this method because it has been reported to be insensitive to data nonstationarities and usable in short data sets (20). Accordingly, in the current study, SOD varied minimally with changes in data set size, and differences between survivors and nonsurvivors were significant in the 800- and 100-beat data sets (Fig. 4).

Stationarity

Data stationarity is an important factor in assessing any signal. A stationary signal is one in which, for example, the mean and SD do not change over time (the heart rate may oscillate, but the mean value stays constant from the beginning to the end of the data set). Although no EKG is perfectly stationary in this sense, the shorter the signal section, the more stationary it must be. This concept is confirmed by the results of this work because for both nonsurvivors and survivors, data became more stationary with shortening of signal lengths. This feature may be an additional advantage of analyzing short "snapshots" of stationary waveform data.

Time- and frequency-domain analysis

In contrast to the complexity-based metrics previously discussed, frequency-domain metrics quantify the strength of the regularly occurring, periodic oscillations in the heart rate. We applied standard time- and frequency-domain analysis in this study. The time-domain metrics remained stable with data set length reductions but failed to provide any discriminatory information between survivors and nonsurvivors. The frequency-domain metric LF separated the two groups in the 100-beat data sets, but considering the high intergroup variability of its values with data set length reductions, this finding may be spurious. We also used CDM (27) to calculate the time-dependent changes in amplitude (HFA) of the high-frequency oscillations. HFA was higher in survivors in 400-beat and shorter data sets. Comparing the two methods (Table 3), we found that in contrast to the frequency-domain values, the HFA CDM values were remarkably consistent across data sets of different sizes. This observation reinforces the concept that the latter method (HFA) is less affected by changes in data set length, by changes in the stationarity of the data set, or by other methodological problems (27). Thus, we are encouraged by this finding to continue to examine the utility of CDM for analysis of heart-rate variability.

Perspective

The most significant methodological limitation in heart-rate variability analysis is the fact that, as of yet, most analysis has been performed only on EKGs with minimal amounts of ectopy. In reality, exclusion of data that contain ectopic beats may constitute loss of valuable information. The presence of ectopic beats in the EKG may signify perturbed physiology, and investigation of several tools from nonlinear dynamics as applicable to data with unfiltered ectopy is currently underway in our laboratory.

The findings in this study need to be confirmed in larger numbers of patients with diverse types of injuries. Our current effort in this regard is 3-fold. First, because civilian trauma patients may be different from combat casualties, data will be collected from combat casualties and a similar analysis performed. Second, the entropy calculation will be provided in real time via custom vital-signs monitors using continuous sliding-window analysis to assess the use of the metric in clinical trauma care. One of the important results of the current work in this regard is establishment of the minimum data set size (window width) to be used in continuous real-time analysis. Third, the use of the newer metrics (SOD and HFA, in particular) will continue to be explored.

Currently, direct contact with the patient and traditional vital signs (heart rate, blood pressure, oxygen saturation) are cornerstones of diagnosis in both combat and civilian settings. Our work may permit assessment of the critically ill without hands-on contact. In the combat setting, due to hostile fire, it may be too risky for the medic to approach a casualty until the scene is safe—unless the casualty is likely to benefit from an immediate life-saving intervention. Under these circumstances, a 100- to 200-heartbeat "snapshot" of the casualty's condition, transmitted from sensors incorporated into the soldier's gear, may be all that is available for remote guidance to the medic. In civilian settings, these new vital signs may improve the accuracy of prehospital triage decisions.

CONCLUSION

Heart-rate complexity is decreased in nonsurviving prehospital trauma patients when compared with survivors. This finding has been confirmed for data sets ranging in size from 800 down to 100 beats by several computationally different metrics from nonlinear dynamics. In particular, evaluation using SampEn, SOD, and CDM was useful in identifying nonsurviving trauma patients from 100-beat-long sections of EKG. Evaluation of HRC using nonlinear metrics may be useful for rapid diagnosis of severity of injury under emergency conditions in trauma patients.

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